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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,006	06/29/2001	Gregory T. Bleck	GALA-06415	1148

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,006	BLECK, GREGORY T.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/1/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,28, 30 and 34-41* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25,28 and 34-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to a request for continued examination and an amendment filed 3/1/04. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/1/04 has been entered.

Claims 21 and 35 have been amended. Claims 26-27, 29 and 31-33 have been cancelled. Claims 1-25, 28, 30 and 34-41 are pending in this application. Claims 1-20 and 30 have been withdrawn. Therefore, claims 21-25, 28 and 34-41 are under examination in this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants recite a vector for expression of first and second immunoglobulin coding sequences which further comprises a bovine/human hybrid alpha-lactalbumin promoter. As

such, the claim reads on a genus of promoters comprising portions of bovine and human lactalbumin promoter sequences.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

The disclosure teaches that a hybrid alpha lactalbumin promoter can be constructed from portions of bovine and human alpha lactalbumin promoter sequences. Applicants teach specifically a bovine/human lactalbumin promoter of SEQ ID NO 1 comprised of bovine promoter sequences from –550 to –2000 and human promoter sequences from +15 to –600. The disclosure of this single species is not accompanied by a disclosure as to the relative properties of these portions and their ability to regulate transcription according to the instant invention. Therefore, there is no clear description of the structural or functional characteristics required for portions of bovine and human lactalbumin promoter sequences to be a hybrid promoter. Neither applicant nor the prior art provide a correlation between the structure of the recited promoter portions and their ability to function in a hybrid promoter. Given the large size and diversity of bovine and human lactalbumin promoter portions and the inability to envision which will also have essential elements required of a hybrid promoter, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not

represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-41 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34-35, and by dependency claims 36-41, are vague and indefinite in that the metes and bounds of "an internal ribosome entry signal operably linked to a nucleic acid encoding a signal sequence" are unclear. Are the first and second coding sequences operably linked to a signal sequence or one of the two.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Kingsman et al, (WO 98/55607; see entire document).

Kingsman et al teach generation of an expression vector for the expression of a protein of interest (POI). This POI is preferably secretable and contains a signaling entity (see e.g. page 12,

paragraph 3). Specifically, Kingsman et al teach that antibody light and heavy chains of the 5T4 antibody (see e.g. page 7, paragraph 5) can be expressed from a retroviral vector (see e.g. page 13, paragraph 5). In this vector, heavy and light chain translation cassettes are separated by an IRES (see e.g. bridging paragraph 46-47). Kingsman et al teach pseudotyping of retroviral vector for expanded tropism (see e.g. page 19, last paragraph through page 22, first paragraph). Absent evidence to the contrary, no special steps are provided for the expression of subunits in about a 0.9:1.1 ratio. Rather, an IRES sequence is used to express a single transcript from which both immunoglobin coding sequences are translated. The resultant ratio appears to be an inherent result of the design of a vector comprised of a heavy and light immunoglobin chain separated by the IRES, a fact which is suggested by the experimental disclosure of the instant invention as illustrated in examples 1 and 6-16. Absent evidence to the contrary, as equimolar ratios of the heavy and light chains are required for immunoglobulin assembly.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piechaczyk et al. (WO 98/31808; see US application 2002/0168339 for English translation; see entire document) in view of Burns et al (US 5,512,421; see entire document).

Applicants claim a method for producing immunoglobulins comprising providing a host cell and a pseudotyped retroviral vector in which a first and second immunoglobulin chain are separated by an IRES such that the first and second chains are expressed at a ratio of 0.9:1:1 to 1:1. The immunoglobulin is secreted.

Piechaczyk et al teach methods for the production of functional Tg10 antibody from PM130, which is a vector comprised of the heavy and light chains of TG10 separated by an IRES (see e.g. table 1 and paragraph 076). PM130 is based upon pLXPXSN, a MLV based retrovirus vector, (see e.g. paragraph 0070) and is grown in PA317 cells, which are amphotropic retroviral packaging cells. Absent evidence to the contrary, no special steps are provided for the expression of subunits in about a 0.9:1.1 ratio. Rather, an IRES sequence is used to express a single transcript from which both immunoglobin coding sequences are translated. The resultant ratio appears to be an inherent result of the design of a vector comprised of a heavy and light immunoglobin chain separated by the IRES, a fact which is suggested by the experimental disclosure of the instant invention as illustrated in examples 1 and 6-16. Absent evidence to the contrary, as equimolar ratios of the heavy and light chains are required for immunoglobulin assembly. Piechaczyk et al teach that the antibody is secreted into the blood circulation (see e.g. paragraph 0018).

Piechaczyk et al do not teach generation of a pseudotyped retroviral vector.

Burns et al teach methods for the generation of vesicular stomatitis virus G glycoprotein (VSV-G) pseudotyped retroviral vectors i.e. LGRNL(VSV-G). In this vector, the G glycoprotein of VSV was inserted into the vector (see e.g. abstract and figure 1). The retrovirus LSRNL comprised of MLV env, pol and gag proteins were produced from PA317 cells, packaging cells

expressing MLV pol, gag and env while the retrovirus LGRNL (VSV-G) comprised of amphotropic pol and gag and VSV-G env was produced from 293 packaging cells expressing pol and gag but lacking env protein (column 27, line 4-63). The efficiency of infection of different cell types was assayed using each vector (see e.g. table 7). LGRNL(VSV-G) cell exhibited a wide and varied host range infecting mammalian and non-mammalian hosts i.e. fish lines and mosquito cell lines. Furthermore, high viral titers were achieved following concentration of viral stocks (see e.g. table 8).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the amphotropic retroviral vector taught by Piechaczyk et al for expression of antibody light and heavy chains separated by an IRES with the VSV-G pseudotyped vector taught by Burns et al because Burns et al teach that it is within the ordinary skill of the art to develop a pseudotyped retroviral vector comprising an envelope sequence from an unrelated virus and because Piechaczyk et al. teach that it is within the ordinary skill of the art to clone and express antibody coding sequences from a retroviral vector. One would have been motivated to do so in order to receive the expected benefit of altered host range of the retroviral particle and higher concentration of viral stocks (see e.g. Burns et al column 6, line 64-67, table 7 and table 8). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

GERRY LEFFERS
PRIMARY EXAMINER

March 11, 2004